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PROGRESS REPORT

INTRODUCTION: Early research indicates that a factor released from contracting muscles causes tumor regression. We have repeatedly observed that exercise slows tumor growth rate, resulting in smaller tumors. We will examine the hypothesis that **a tumoristatic factor is released by contracting muscles**. Soleus (slow-oxidative) and flexor digitorum brevis (fast-glycolytic) muscles of Wistar rats will be excised, maintained in Krebs Heinsleit buffer, and attached by electrodes to a force transducer. To fatigue, moderate, and no stimulation protocols will be performed to test a dose response effect. The buffer and effluent from individual muscles will be dialyzed, lyophilized and resuspended in saline. Extracts will be tested for growth effects in MCF-7 and MDA-MB-231 cells using 5-bromo-2-deoxyuridine incorporation and TUNEL assays. Growth-inhibiting and control extracts will be injected subcutaneously into female BALB/c nude mice, implanted with ER+ or ER- breast tumor cells, after tumors have reached 1 cm³. Tumor size will be measured 3 times/week and animals sacrificed after 2-6 weeks. Tumors will be excised, weighed, then portions frozen and fixed to determine proliferation and apoptotic indices. Extract aliquots will be frozen at -80°C for future characterization of the tumoristatic factor(s). This work has important implications for prevention and treatment of breast cancer, including: identification of a mechanism for exercise-mediated tumor inhibition, identification of a marker to assess efficacy of an exercise program to inhibit tumorigenesis, and identification of a therapeutic intervention, using the tumoristatic factor pharmacologically, or through an exercise program to release the factor into circulation.

BODY: As of Sept 1, 2006 the projects had not commenced due to the merger between the AMC Cancer Center and the University of Colorado Health Sciences. This merger and the associated difficulties with transferring grants halted progress on the grant

KEY RESEARCH ACCOMPLISHMENTS: PI met with consultant Jim Fluckey, Ph.D from Texas A&M in April 2006 to discuss research design and study time line.

REPORTABLE OUTCOMES: None to date

CONCLUSION: The extension year will provide us with all the information for this grant

REFERENCES: NA

APPENDICES: NA

SUPPORTING DATA: NA